

**IN THE SPECIFICATION:**

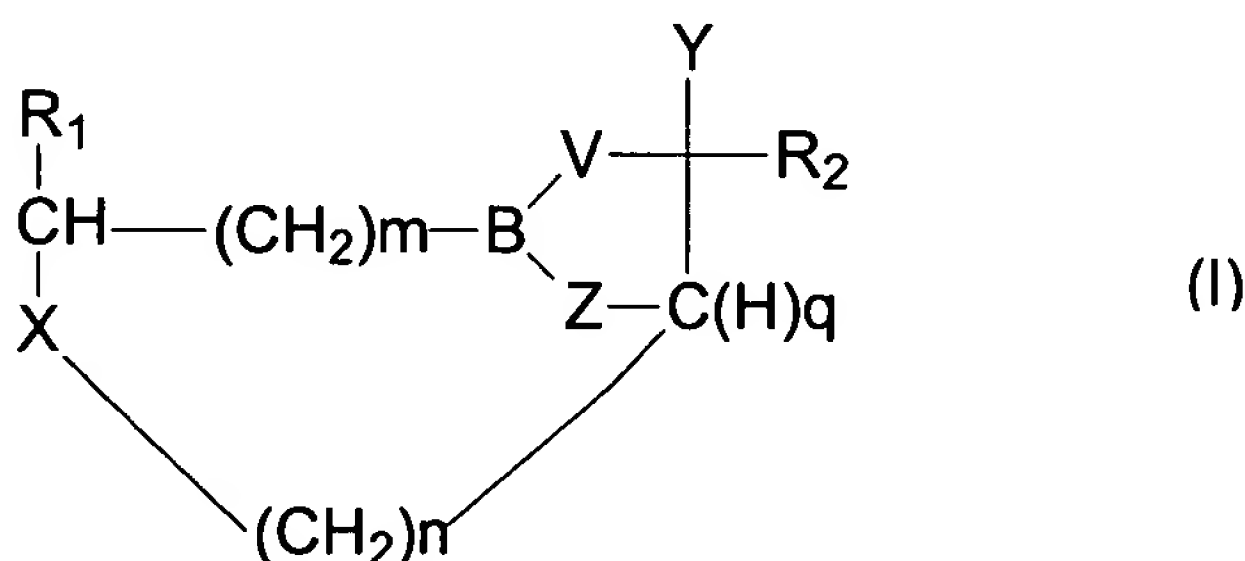
Under Field Of The Invention, delete second paragraph on page 2 and substitute the following paragraph:

C<sup>1</sup> This application is a continuation of Application Ser. No. 08/333,237, filed November 2, 1994, *now U.S. Patent 5,952,462* which is a continuation of Application Ser. No. 07/190,271, filed ~~June~~ *May* 4, 1988, now abandoned, which was a continuation-in-part of Application Ser. No. 674,253, filed November 27, 1984, *now U.S. Patent 4,888,281* which was a continuation-in-part of application Ser. No. 556,016, filed November 29, 1983, now abandoned, the contents of which applications are hereby incorporated by reference into this application.

The changes in this paragraph includes no new matter.

**IN THE CLAIMS:**

36. (Amended) A catalytic antibody elicited by an antigen comprising the boron-containing hapten of formula I,



wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy

protecting group, a primary amido containing side chain of a naturally occurring amino acid

wherein said amido group may be glycosylated, (C<sub>2</sub>-C<sub>4</sub>) alkyl, -CH<sub>2</sub>CH(CO<sub>2</sub>H)<sub>2</sub>,

-(CH<sub>2</sub>)<sub>2</sub> S(O)CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub> S(O)<sub>2</sub> CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub> NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>3</sub> ONHC(=NH)NH<sub>2</sub>;

V is O, CH<sub>2</sub> or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group,

amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond,

amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-

C<sub>9</sub>) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl,

wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted

by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a

carbonyl bonded to the N terminus of a peptide through a peptide bond, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-

C<sub>9</sub>)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein

the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by

halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl; and wherein

Z is O, CH<sub>2</sub> or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

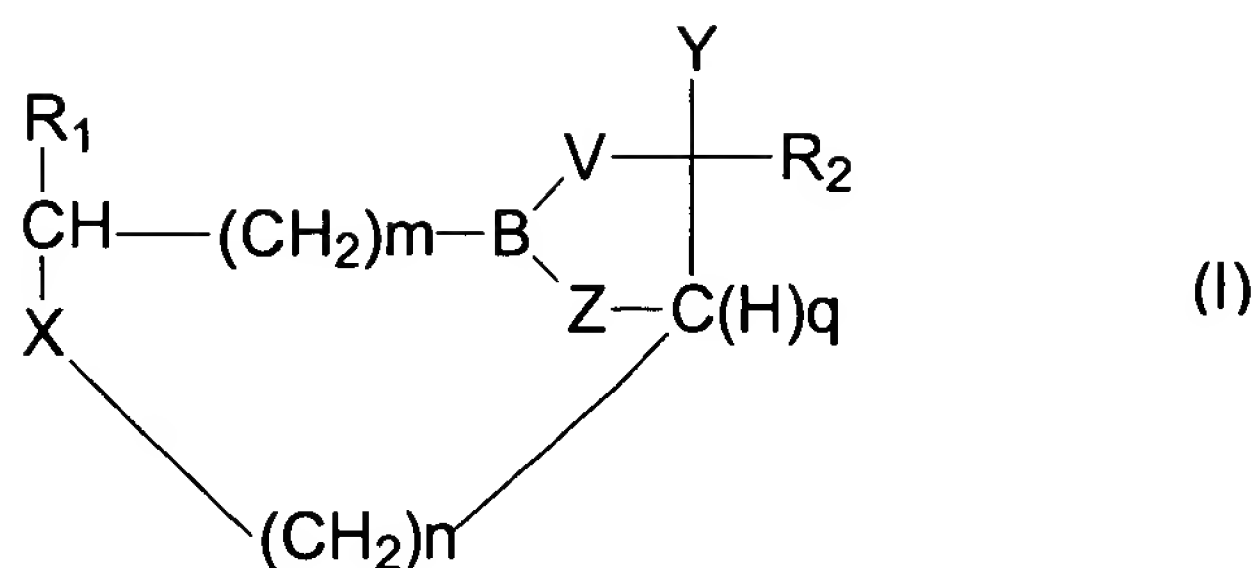
q is 1 or 2 provided that if q is 2, then n=0 and there is no bond

between X and the carbon bound to Z.

39. (Twice Amended) A catalytic antibody which catalyzes a chemical reaction of

interest and which is elicited through *in vitro* or *in vivo* techniques by an antigen comprising the

boron-containing hapten of formula I,



wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C<sub>2</sub>–C<sub>4</sub>) alkyl, –CH<sub>2</sub>CH(CO<sub>2</sub>H)<sub>2</sub>, –(CH<sub>2</sub>)<sub>2</sub> S(O)CH<sub>3</sub>, –(CH<sub>2</sub>)<sub>2</sub> S(O)<sub>2</sub> CH<sub>3</sub>, –(CH<sub>2</sub>)<sub>3</sub> NH<sub>2</sub> or –(CH<sub>2</sub>)<sub>3</sub> ONHC(=NH)NH<sub>2</sub>;

V is O, CH<sub>2</sub> or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C<sub>1</sub>–C<sub>9</sub>)alkyl, (C<sub>1</sub>–C<sub>9</sub>) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>–C<sub>4</sub>)alkoxy or (C<sub>1</sub>–C<sub>4</sub>)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C<sub>1</sub>–C<sub>9</sub>)alkyl, (C<sub>1</sub>–C<sub>9</sub>)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>–C<sub>4</sub>)alkyl, (C<sub>1</sub>–C<sub>4</sub>)alkoxy or (C<sub>1</sub>–C<sub>4</sub>)alkoxycarbonyl; and wherein

Z is O, CH<sub>2</sub> or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

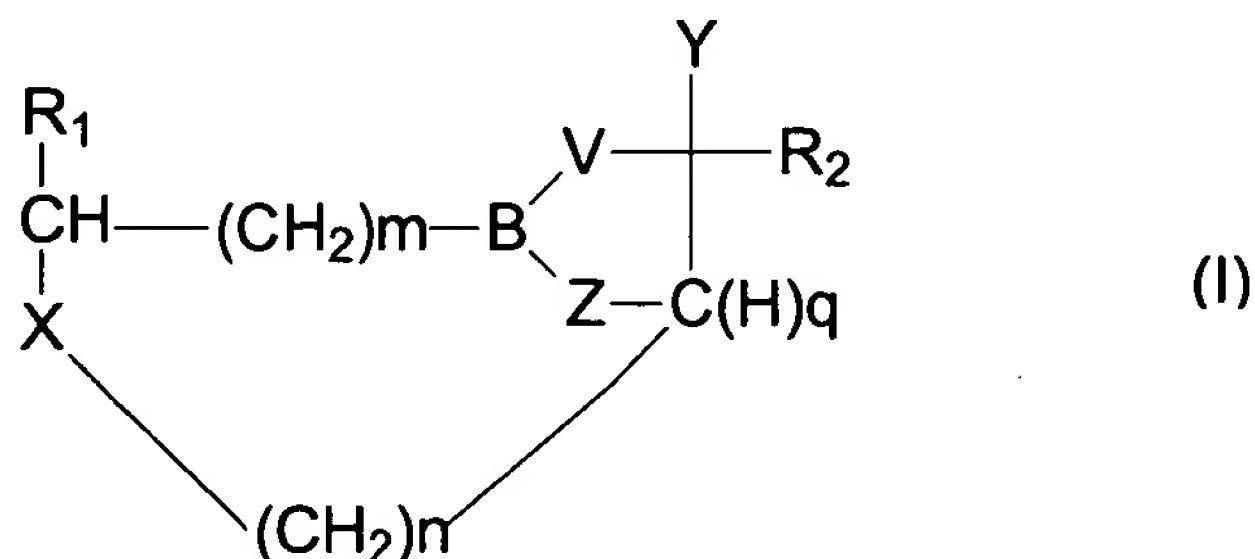
q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

<sup>C<sup>3</sup></sup>  
encl. said catalytic antibody having been prepared by a process comprising the steps of:

- (a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;
- (b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and
- (c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

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42. (Twice Amended) A method for producing catalytic antibodies which catalyze a chemical reaction of interest and which are elicited through *in vitro* or *in vivo* techniques by an antigen comprising the boron-containing hapten of formula I,



wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said

hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C<sub>2</sub>-C<sub>4</sub>) alkyl, -CH<sub>2</sub>CH(CO<sub>2</sub>H)<sub>2</sub>, -(CH<sub>2</sub>)<sub>2</sub> S(O)CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub> S(O)<sub>2</sub> CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub> NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>3</sub> ONHC(=NH)NH<sub>2</sub>;

V is O, CH<sub>2</sub> or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-C<sub>9</sub>)alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-C<sub>9</sub>)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl; and wherein

Z is O, CH<sub>2</sub> or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

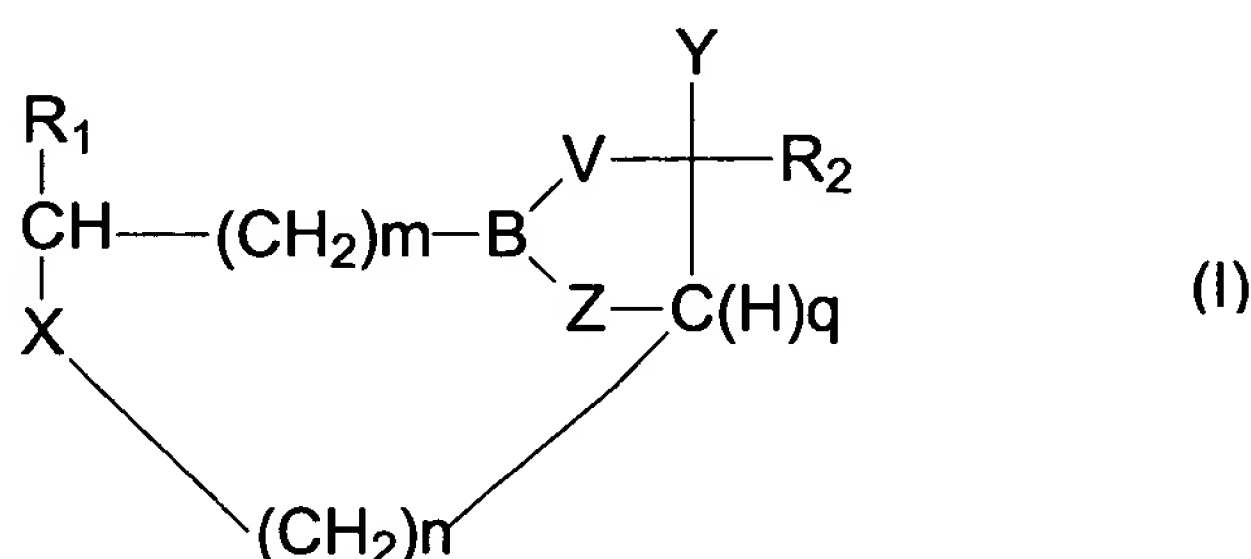
wherein said method comprises the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

45. (Amended) A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the boron-containing hapten of formula I,



wherein

R<sub>1</sub> and R<sub>2</sub> may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C<sub>2</sub>-C<sub>4</sub>) alkyl, -CH<sub>2</sub>CH(CO<sub>2</sub>H)<sub>2</sub>, -(CH<sub>2</sub>)<sub>2</sub> S(O)CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub> S(O)<sub>2</sub> CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub> NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>3</sub> ONHC(=NH)NH<sub>2</sub>;

V is O, CH<sub>2</sub> or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-

C<sub>9</sub>) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C<sub>1</sub>-C<sub>9</sub>)alkyl, (C<sub>1</sub>-C<sub>9</sub>)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy or (C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl; and wherein

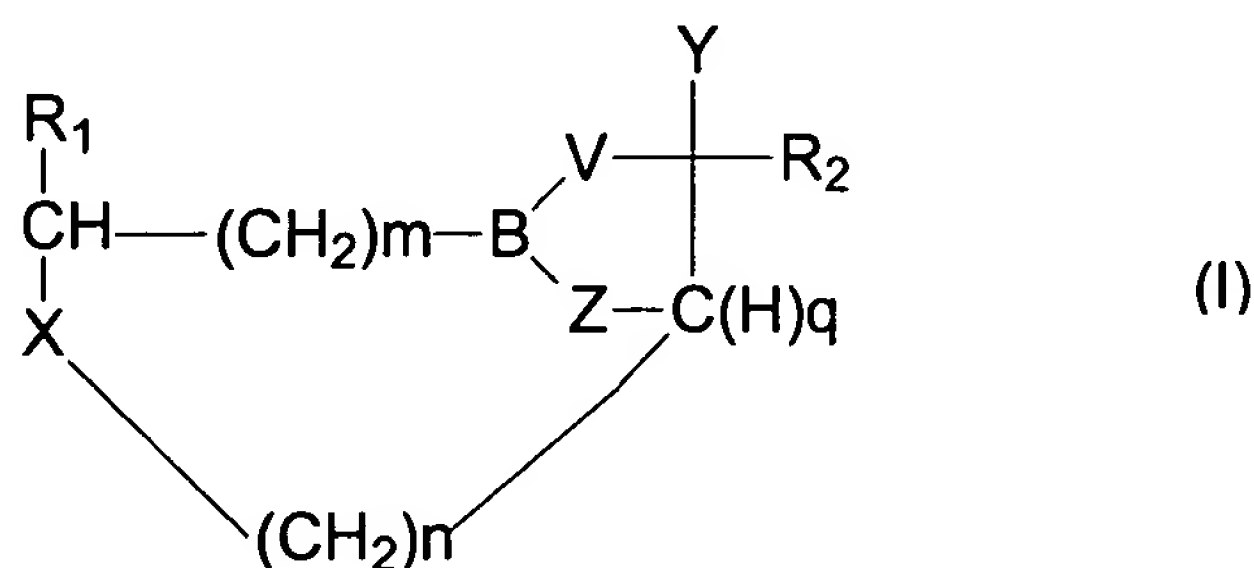
Z is O, CH<sub>2</sub> or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

48. (Twice Amended) A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises: contacting said molecule with an effective amount of a catalytic antibody elicited with a boron-containing hapten of formula I,



wherein

$R_1$  and  $R_2$  may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated,  $(C_2-C_4)$  alkyl,  $-CH_2CH(CO_2H)_2$ ,  $-(CH_2)_2 S(O)CH_3$ ,  $-(CH_2)_2 S(O)_2 CH_3$ ,  $-(CH_2)_3 NH_2$  or  $-(CH_2)_3 ONHC(=NH)NH_2$ ;

V is O,  $CH_2$  or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene,  $(C_1-C_9)$ alkyl,  $(C_1-C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen,  $(C_1-C_4)$ alkoxy or  $(C_1-C_4)$ alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond,  $(C_1-C_9)$ alkyl,  $(C_1-C_9)$ alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen,  $(C_1-C_4)$ alkyl,  $(C_1-C_4)$ alkoxy or  $(C_1-C_4)$ alkoxycarbonyl; and wherein

Z is O,  $CH_2$  or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then  $n=0$  and there is no bond between X and the carbon bound to Z,

said hapten being homologous to said specific amino acid sequence.